Enclosure No:	**1/AWMSG/1215**
Agenda Item No:	**1** – Minutes of previous meeting
Author:	Chairman, AWMSG
Contact:	Tel: 029 20716900 E-Mail: awttc@wales.nhs.uk

ALL WALES MEDICINES STRATEGY GROUP (AWMSG)

Minutes of the AWMSG meeting held Wednesday, 11th November 2015 commencing 9.30 am at the Park Inn Hotel Cardiff North, Circle Way East Cardiff CF23 9XF

VOTING MEMBERS PRESENT:

			Did not participate in
1.	Dr Stuart Linton	Chair	
2.	Professor John Watkins	Public Health Wales / Vice Chair	
3.	Dr Catherine Bale	Hospital Consultant	
4.	Dr Jeremy Black	General Practitioner	
5.	Dr Geoffrey Carroll	Welsh Health Specialised Services Committee	**13-17**
6.	Mr Stuart Davies	Finance Director	
7.	Professor David Cohen	Health Economist	
8.	Dr Karen Fitzgerald	Public Health Wales	
9.	Dr Emma Mason	Clinical Pharmacologist	**13-17**
10.	Mr Christopher Palmer	Lay Member	
11.	Mr Robert Thomas	ABPI Cymru Wales	**6**
12.	Dr Mark Walker	Medical Director	
13.	Mr Roger Williams	Managed Sector Secondary Care Pharmacist	
14.	Mrs Louise Williams	Senior Nurse	

WELSH GOVERNMENT:
No representation

IN ATTENDANCE:
Dr Saad Al-Ismail, NMG Chair / Mr Scott Peglar, NMG Vice Chair
Mrs Karen Samuels, Head of HTA & Patient Access, AWTTC
Mrs Ruth Lang, Head of Liaison & Administration, AWTTC

AWTTC APPRAISAL LEADS:
Mr Anthony Williams, Senior Appraisal Pharmacist
Mrs Helen Adams, Senior Appraisal Pharmacist
Mrs Gail Woodland, Senior Appraisal Pharmacist
Dr Claire Davis, Senior Appraisal Scientist

List of Abbreviations:

ABPI	Association of the British Pharmaceutical Industry
ASAR	AWMSG Secretariat Assessment Report
AWMSG	All Wales Medicines Strategy Group
AWPAG	All Wales Prescribing Advisory Group
AWTTC	All Wales Therapeutics & Toxicology Centre
BMA	British Medical Association
CAPIG	Clinical and Patient Involvement Group
CEPP	Clinical Effectiveness Prescribing Programme
CHMP	Committee for Medicinal Products for Human Use
DoH	Department of Health
ECDF	English Cancer Drugs Fund
EMA	European Medicines Agency
EOL	End of life
FAR	Final Appraisal Recommendation
FDA	US Food and Drug Administration
GP	General Practitioner
HAC	High Acquisition Cost
HB	Health Boards
HST	Highly Specialised Technology
HTA	Health Technology Appraisal
IR	Independent Review
MHRA	Medicines and Healthcare products Regulatory Agency
MMPB	Medicines Management Programme Board
M&TCs	Medicines & Therapeutics Committees
NICE	National Institute for Health and Care Excellence
NMG	New Medicines Group
PAR	Preliminary Appraisal Recommendation
PAS	Patient Access Scheme
PPRS	Prescription Price Regulation Scheme
SMC	Scottish Medicines Consortium
SPC	Summary of Product Characteristics
TDAPG	Therapeutic Development Appraisal Partnership Group
T&FG	Task and Finish Group
UHB	University Health Board
WAPSU	Welsh Analytical Prescribing Support Unit
WCPPE	Welsh Centre for Pharmacy Postgraduate Education
WeMeReC	Welsh Medicines Resource Centre
WG	Welsh Government
WHO	World Health Organization
WHSSC	Welsh Health Specialised Services Committee
WPAS	Wales Patient Access Scheme

Welcome and introduction

1. The Chairman opened the meeting and welcomed Mr Scott Peglar, NMG Vice-Chair, to his first AWMSG meeting as an observer, and also Ms Mandy James, Senior Nurse deputy member who was observing from the public gallery.

2. Apologies

Mrs Alison Hughes and Mrs Susan Murphy (Managed Sector Primary Care Pharmacist)
Mr Alun Morgan and Mr Scott Cawley (Other professions eligible to prescribe)
Mr Stefan Fec (Community Pharmacist)
Professor Roger Walker (Chief Pharmaceutical Officer, Welsh Government)

3. Declarations of interest

The Chairman invited declarations of interest pertinent to the agenda. Mr Robert Thomas declared a personal specific interest in relation to the appraisal of insulin glargine (Abasaglar®). The Chairman confirmed that Mr Thomas would be required to leave the meeting and would not participate in the appraisal or vote.

4. Minutes of previous meeting

The minutes of the previous meeting were checked for accuracy and approved.

5. Chairman's report

The Chairman confirmed that following the negative recommendation of tiotropium (Spiriva® Respimat®) at the previous AWMSG meeting the marketing authorisation holder, Boehringer Ingelheim Limited, requested an independent review (IR). Members were informed that the grounds for this IR request are currently being considered and the appraisal process has been suspended. The Chairman confirmed that with the exception of tiotropium (Spiriva® Respimat®) the recommendations announced at AWMSG's meeting in October had been submitted to Welsh Government. AWTTC are awaiting confirmation of ministerial ratification.

The Chairman reported that following receipt of NMG's recommendation not supporting use of ivacaftor (Kalydeco®) for the treatment of cystic fibrosis (CF) in patients age 6 years and older who have one of the following gating (class III) mutations in the CFTR gene: G1244E, G1349D, G178R, G551S, S1251N, S1255P, S549N, or S549R, the marketing authorisation holder, Vertex Pharmaceuticals Limited, had requested a meeting of the Clinical and Patient Involvement Group (CAPIG). Members were informed that the first CAPIG meeting was held on Wednesday, 28th October and appraisal by AWMSG would be undertaken in December. With regard to cetuximab (Erbitux®)for the treatment of patients with epidermal growth factor receptor (EGFR)-expressing, RAS wild-type metastatic colorectal cancer, in combination with irinotecan-based chemotherapy, in first-line in combination with FOLFOX, as a single agent in patients who have failed oxaliplatin- and irinotecan-based therapy and who are intolerant to irinotecan, the Chairman informed members that the marketing authorisation holder, Merck Serono Limited, had requested a meeting to explore issues relating to AWMSG's policy for appraising medicines at the end of life. A panel meeting convened on 4th November and appraisal by AWMSG would be undertaken in December.

The Chairman highlighted that the process for appraising limited submissions had recently been reviewed and it is intended that a more streamlined process will be introduced from December 2015. The Chairman reminded members that if an application is considered eligible for a limited submission, only evidence of clinical-effectiveness and budget impact compared to existing comparator products(s) is provided by the marketing authorisation holder. No evidence of cost-effectiveness is required. Members were informed that the ASAR template for limited submissions had been updated; providing a brief summary of information which, once ratified by Welsh Government, would be made available on the AWMSG website alongside the final appraisal recommendation. The Chairman confirmed that the New Medicines Group's

preliminary recommendation will continue to be presented to AWMSG for consideration along with the ASAR, however, full discussion is not anticipated unless an outstanding issue is identified by AWMSG. The Chairman clarified that whilst there is no expectation that the applicant company will attend, if they choose to do so they will be invited to join the meeting and respond to any issues, if input is required. The Chairman stated that he would continue to seek confirmation that the process had been fair and transparent. In circumstances where a medicine had been considered eligible for a full submission, but the marketing authorisation holder provided a limited submission, then this would be highlighted to NMG and AWMSG and more detailed scrutiny of the submission would be required. The Chairman confirmed that the Form C may be made available to members for background information purposes only.

The Chairman announced the pending retirement of Dr Geoffrey Carroll and Professor David Cohen and confirmed their last AWMSG meeting in December. The Chairman thanked Dr Carroll and Professor Cohen for their valued expertise, diligence and excellent contribution over many years. Members were informed that Professor Dyfrig Hughes would be taking up the role as AWMSG's Health Economist and will no longer have input as AWTTC's Health Economist. The Chairman is currently awaiting a nomination from WHSSC.

The Chairman announced the appraisals scheduled for the next AWMSG meeting to be held on Wednesday, 9th December 2015 in Abergavenny. In addition to the appraisal of ivacaftor and cetuximab, the following appraisals will be undertaken:

Full Submissions:

Macitentan (Opsumit®) as monotherapy or in combination, for the long-term treatment of pulmonary arterial hypertension (PAH) in adult patients of WHO Functional Class (FC) II to III
Applicant Company: Actelion Pharmaceuticals UK Ltd

Empagliflozin (Jardiance®) for the treatment of type 2 diabetes mellitus to improve glycaemic control in adults as monotherapy when diet and exercise alone do not provide adequate glycaemic control in patients for whom use of metformin is considered inappropriate due to intolerance
Applicant Company: Boehringer Ingelheim Ltd

Limited submissions:

Efavirenz (Sustiva®) indicated in antiviral combination treatment of human immunodeficiency virus-1 (HIV-1) infected children 3 months of age and weighing at least 3.5 kg to children 3 years of age
Applicant Company: Bristol-Myers Squibb Pharmaceuticals Ltd

Atazanavir/cobicistat (Evotaz®) in combination with other antiretroviral medicinal products for the treatment of HIV-1 infected adults without known mutations associated with resistance to atazanavir
Applicant Company: Bristol-Myers Squibb Pharmaceuticals Ltd

Members were reminded to declare any interests in relation to these appraisals before the next meeting. Patients, patient organisations and patient carers were invited to submit their views to AWTTC in relation to medicines scheduled for appraisal.

6. Appraisal 1: Full Submission
Insulin glargine (Abasaglar®) for the treatment of diabetes mellitus in adults, adolescents and children aged 2 years and above

The Chairman welcomed representation from Boehringer Ingelheim and Eli Lilly & Co Ltd.

Mr Rob Thomas left the meeting. The Chairman invited members to declare any interests in either the applicant company or the medicine if they had not already done so. No further interests were declared.

The Chairman announced that AWMSG advice has no impact on the licensed status of the technology and the inherent implications associated with this. A negative recommendation would not impact on the clinical freedom of the prescriber. It was noted that a positive recommendation by AWMSG, subsequently endorsed by Welsh Government, places an obligation on Health Boards to fund accordingly. It was confirmed that AWMSG advice is interim to final NICE guidance should this be subsequently published. The Chairman outlined the sequence of events and invited Mrs Helen Adams, AWTTC Appraisal Lead, to set the context of the appraisal.

Mrs Adams presented an overview of the submission as detailed in the ASAR. The Chairman invited Dr Saad Al-Ismail, the NMG Chairman, to provide a brief overview of the relevant issues identified in the preliminary appraisal. Dr Al-Ismail confirmed that a preliminary appraisal had been undertaken on 7th October and the view of NMG was that insulin glargine (Abasaglar®▼) should be supported for use as an option for restricted use within NHS Wales for the treatment of diabetes mellitus in adults, adolescents and children aged 2 years and above. It was the view of NMG that insulin glargine (Abasaglar®▼) should be prescribed within its licensed indication in accordance with NICE or AWMSG guidance for insulin glargine (Lantus®), the reference product. NMG advised that it should be prescribed by brand name to avoid automatic substitution and therefore help with pharmacovigilance. Dr Al-Ismail clarified NMG's view that insulin glargine (Abasaglar®▼) should not be recommended for use within NHS Wales outside of these circumstances.

The Chairman opened the discussion in relation to clinical effectiveness. Members sought clarification in relation to the presentation of the product, number of units/clicks required and dosing, and in particular, with regards to the reference medicine. Mrs Adams relayed the views of the clinical experts and confirmed their broad support for the availability of biosimilar basal analogue insulins, with an assumed reduction of acquisition cost. Mrs Adams highlighted the experts' view that a widespread 'switch' based on cost alone would be clinically inappropriate and the importance of prescribing insulin by brand. She highlighted the unmet need identified in the clinical expert summary and referred to relevant NICE clinical guidelines.

The Chairman invited Professor Cohen to comment on the case for cost-effectiveness. Professor Cohen confirmed his role as AWMSG health economist and assured the company delegates that he had no involvement in compiling the ASAR or discussions at NMG. Professor Cohen provided an overview of the case presented, as summarised in the ASAR. When referring to the cost minimisation analysis, he reiterated the requirement to assume equivalence across all health domains and accepted that it was an appropriate analysis for this biosimilar medicine. He offered the company delegates opportunity to correct or comment on any aspect of his summary. The Chairman drew members' attention to the budget impact evidence in the ASAR. Members sought clarification of the source of the company estimates in relation to the number of eligible patients in NHS Wales.

The Chairman highlighted the role of the lay member in ensuring that patient, carer and public views and experiences inform AWMSG. He referred members to the two patient organisation questionnaires and confirmed that all members had received and read the documentation. For the purposes of transparency Mr Palmer highlighted the salient aspects of the patient questionnaires received from Diabetes UK Cymru and InDependent Diabetes Trust. The potential safety risks and adverse events associated with insulin treatments were highlighted. Mr Palmer stated that patients need insulins which offer the greatest flexibility in order to manage their medication and live as normally as possible, with good glucose control and low risk of hypoglycaemia. It was noted that this is the first biosimilar insulin and the potential

advantages and disadvantages. The wider societal impact of hypoglycaemia on productivity and costs for both employers and employees was noted.

The Chairman referred to the applicant company's response and offered further opportunity for the company delegate to comment prior to concluding the appraisal. Having received confirmation that the appraisal process had been fair and transparent and that all relevant issues had been discussed, the Chairman closed the appraisal.

Appraisal decision subsequently announced in public:
The Chairman confirmed that having read the evidence and considered the various issues that arose during the discussion, the following recommendation would be forwarded to Welsh Government:

Insulin glargine (Abasaglar®▼) is recommended as an option for restricted use within NHS Wales for the treatment of diabetes mellitus in adults, adolescents and children aged 2 years and above.

Insulin glargine (Abasaglar®▼) should be prescribed within its licensed indication in accordance with NICE or AWMSG guidance for insulin glargine (Lantus®), the reference product.

Insulin glargine (Abasaglar®▼) is not recommended for use within NHS Wales outside of these circumstances.

Insulin glargine (Abasaglar®▼) should be prescribed by brand name to avoid automatic substitution and therefore help with pharmacovigilance.

The Chairman announced that confirmation of AWMSG's recommendations would be forwarded to applicant companies within five working days. He informed company delegates that they had up to ten working days to accept the recommendation or lodge a request for an independent review. It was noted that failure to respond within the deadline would not delay the process.

7. Appraisal 2: Full Submission

Sucroferric oxyhydroxide (Velphoro®▼) for the control of serum phosphorus levels in adult chronic kidney disease (CKD) patients on haemodialysis (HD) or peritoneal dialysis (PD). Sucroferric oxyhydroxide (Velphoro®▼) should be used within the context of a multiple therapeutic approach, which could include calcium supplement, 1,25-dihydroxy vitamin D3 or one of its analogues, or calcimimetics to control the development of renal bone disease

The Chairman welcomed delegates from the applicant Company, Fresenius Medical Care UK Ltd. Mr Rob Thomas joined the meeting.

The Chairman reminded members to declare any interests in either the applicant company or the medicine if they had not already done so. No further interests were declared.

The Chairman referred to his previous statement regarding the impact of AWMSG advice on the licensed status of the technology and the inherent implications associated with this, and invited Dr Claire Davis, the AWTTC Appraisal Lead, to set the context of the appraisal.

Dr Davis presented an overview of the submission as detailed in the ASAR. Dr Saad Al-Ismail, provided a brief overview of the relevant issues identified in the preliminary appraisal. Dr Al-Ismail relayed the view of NMG that sucroferric oxyhydroxide (Velphoro®▼) should be recommended as an option for restricted use within NHS Wales sucroferric oxyhydroxide (Velphoro®▼) when non-calcium based phosphate binders are considered appropriate. Dr Al-

Ismail informed members that the cost-effectiveness evidence provided by the applicant company was limited to second-line use in adults whose serum phosphorus levels are not controlled with a calcium-based binder or who are controlled but have high serum calcium levels or low serum parathyroid levels, in line with the recommendations for the use of non-calcium phosphate binders in guidelines for hyperphosphataemia in chronic kidney disease.

The Chairman opened the discussion and members discussed issues relating to clinical effectiveness. Members sought clarification in relation to the adverse event profile and there was discussion in relation to pill burden and compliance. The clinical relevance of the end points was discussed and members asked the industry delegates to provide the rationale for starting patients on a lower dose than that recommended in the SPC. The Chairman referred to the clinical expert summary. Experts considered that sucroferric oxyhydroxide would sit alongside sevelamer and lanthanum as a calcium-free binder. Experts also highlighted that phosphate binders are beset with problems of poor adherence to treatment and therefore an additional option would be welcomed. Cost was considered to be a key issue.

The Chairman invited Professor Cohen to comment on the case for cost-effectiveness. Professor Cohen confirmed his role as AWMSG health economist and confirmed he had no involvement in compiling the ASAR or in discussions at NMG. Professor Cohen summarised the case presented and sought clarification that there was therapeutic equivalence across all domains. The company delegates were asked provide the rationale for their choice of comparator and highlighted the limitations and uncertainties in their submission. There was discussion in relation to the budget impact and clarification was sought in relation to the number of eligible patients in Wales.

The Chairman asked the lay member, Mr Chris Palmer, to highlight the salient issues highlighted in the patient organisation questionnaires from Kidney Research UK and the National Kidney Federation. Mr Palmer stated that treatment choice is essential as many patients struggle to manage their illness because of the high pill burden. An additional treatment offering a more palatable and flexible dosing option would improve patient compliance and adherence. It was noted that for patients and their carers the management of the disease is challenging and time consuming. Members acknowledged their responsibility in working within the prudent healthcare agenda; however, it was recognised that for any clinical condition a wide range of treatment options is required. Mr Stuart Davies offered to relay the discussion via the Wales Renal Network.

The Chairman referred to the company response to the preliminary recommendation and invited the company delegates to comment. Prior to concluding the appraisal proceedings he asked the company delegates to confirm they were satisfied that all issues had been adequately addressed and taken into account, and that the process had been fair and transparent. The Chairman concluded the appraisal proceedings.

Appraisal decision subsequently announced in public:
The Chairman confirmed that having read the evidence and considered the various issues that arose during the discussion, the following recommendation would be forwarded to Welsh Government:

Sucroferric oxyhydroxide (Velphoro®▼) is recommended as an option for restricted use within its licensed indication within NHS Wales for the control of serum phosphorus levels in adult chronic kidney disease (CKD) patients on haemodialysis (HD) or peritoneal dialysis (PD). Sucroferric oxyhydroxide (Velphoro®▼) should be used within the context of a multiple therapeutic approach, which could include calcium supplement, 1,25-dihydroxy vitamin D3 or one of its analogues, or calcimimetics to control the development of renal bone disease.

Sucroferric oxyhydroxide (Velphoro®▼) should be restricted as an option for use where non-calcium based phosphate binders are considered appropriate

Sucroferric oxyhydroxide (Velphoro®▼) is not recommended for use within NHS Wales outside of this subpopulation.

The Chairman announced that confirmation of AWMSG's recommendations would be forwarded to applicant companies within five working days. He informed company delegates that they had up to ten working days to accept the recommendation or lodge a request for an independent review. It was noted that failure to respond within the deadline would not delay the process.

8. Monitoring Usage in Wales of Medicines Appraised by NICE and AWMSG – Data to March 2015

Mrs Kate Jenkins, Senior WAPSU Pharmacist, presented a report analysing NHS Wales usage of medicines appraised by NICE and AWMSG and medicines not endorsed for use because the marketing authorisation holder had not provided a submission. Mrs Jenkins clarified that the report relates to positive and negative advice issued between April 2003 and 31 March 2015, and medicines usage data are reported for the period 1 April 2012 to 31 March 2015.

Members welcomed the paper and agreed that it provided a valuable resource tool for individual health boards. There was general acknowledgement that there would be a need for each health board to provide the local intelligence in understanding the variance. Dr Al-Ismail suggested that for cancer medicines the Chemocare System in South West Wales would provide the full indication and this might help with the development of a local dataset for a high cost area with a population of 1 million. Concern was expressed over the prescribing of medicines not recommended for use and Mr Stuart Davies agreed to highlight this with his Finance Director colleagues. Suggestions in relation to format and benchmarking were noted. The Chairman closed the discussion by thanking WAPSU for developing a very useful resource.

9. National Prescribing Indicators 2015–2016 – Analysis of Prescribing Data to June 2015

Mrs Kate Jenkins presented the National Prescribing Indicators 2015–2016 Analysis of Prescribing Data to June 2015. She explained that AWMSG had endorsed National Prescribing Indicators (NPIs) as a means of promoting safe and cost-effective prescribing since 2003. Members were informed that for 2015–2016, there are 13 NPIs focusing on eight areas of prescribing and the reporting of adverse events (Yellow Cards). A threshold level of prescribing/reporting is set for 12 of the 13 NPIs. Mrs Jenkins confirmed that the paper reports on NPI prescribing data to June 2015 and is pertinent to the 'Improving Health – Prescribing Guidance' recommendation within AWMSG's Medicines Strategy 2013–2018: AWMSG will work with health boards and other stakeholders to promote the safe, effective and cost-effective use of medicines in Wales.

Members welcomed the report. The scale and variation within the clusters was noted and a suggestion was made that quantification of what might be considered the 'norm' might be helpful to health boards in implementing change. Professor Watkins informed members that the Public Health Wales Observatory provides information on variations in morbidity and relationships between cluster deprivation areas compared with affluent areas. A suggestion was made that it would be useful to find out which health boards had included a NPI as part of their local incentive scheme and this would help identify drivers for change. Mrs Samuels confirmed that AWTTC would be hosting a NPI Information Day so that health board prescribing advisers can share experiences and identify best practice.

10. Appraisal 3 – Full Submission

Tedizolid phosphate (Sivextro®) for the treatment of acute bacterial skin and skin structure infections (ABSSSI) in adults

The Chairman welcomed delegates from the applicant company, Merck Sharp & Dohme Ltd.

The Chairman reminded members to declare any interests in either the applicant company or the medicine if they had not already done so. No interests were declared.

The Chairman referred to his previous statement that AWMSG advice has no impact on the licensed status of the technology and the inherent implications associated with this. A negative recommendation would not impact on the clinical freedom of the prescriber. It was noted that a positive recommendation by AWMSG, subsequently endorsed by Welsh Government, places an obligation on Health Boards to fund accordingly. It was confirmed that AWMSG advice is interim to final NICE guidance should this be subsequently published.

The Chairman outlined the sequence of events and invited Mrs Gail Woodland, AWTTC Appraisal Lead, to set the context of the appraisal. Mrs Woodland presented an overview of the submission as detailed in the ASAR. Dr Saad Al-Ismail relayed the view of NMG that tedizolid phosphate (Sivextro®▼) should be recommended as an option for restricted use within NHS Wales for the treatment of adult patients with acute bacterial and skin structure infections (ABSSSI) caused by Gram-positive *Staphylococcus aureus* (specifically methicillin-resistant [MRSA] isolates) as an alternative oxazolidinione antibacterial. Treatment should only be initiated on advice from local microbiologists or specialists in infectious diseases. NMG were of the opinion that tedizolid phosphate (Sivextro®▼) should not be recommended for use within NHS Wales outside of this subpopulation/circumstance. Members were informed that the applicant company had not submitted evidence on the use of tedizolid phosphate in 'mixed infections' where the infection involves both Gram-positive and Gram-negative organisms.

The Chairman opened the discussion. There were no issues in relation to clinical effectiveness. The Chairman drew attention to the clinical expert views. Mrs Woodland relayed the view of clinical experts that as linezolid can cause bone marrow suppression when used for prolonged periods, an alternative oxazolidinone that did not cause such a problem, or caused it less frequently, would be helpful in managing complicated skin and soft tissue infections.

The Chairman invited Professor Cohen to comment on the case for cost-effectiveness. Professor Cohen confirmed his role as AWMSG health economist and confirmed he had no involvement in compiling the ASAR or in discussions at NMG. Professor Cohen provided an overview of the case presented, as summarised in the ASAR. He had no specific questions and offered the company delegates opportunity to correct or comment on any aspect of his summary. There were no issues of note.

The Chairman drew members' attention to the budget impact evidence in the ASAR and there were no issues of note.

Mr Palmer confirmed that AWTTC had invited comment from two patient organisations; however, no patient organisation submissions had been received. In the absence of any patient views, Mr Palmer highlighted that a once daily dose and shorter duration would be welcomed by patients. There were no outstanding wider societal issues.

The Chairman referred to the applicant company's response and offered further opportunity for the company delegate to comment prior to concluding the appraisal. The delegates had no further comment. Having received confirmation that the appraisal process had been fair and transparent and that all relevant issues had been discussed, the Chairman closed the appraisal.

Appraisal decision subsequently announced in public:
The Chairman confirmed that having read the evidence and considered the various issues that arose during the discussion, the following recommendation would be forwarded to Welsh Government:

Tedizolid phosphate (Sivextro®▼) is recommended as an option for restricted use within NHS Wales for the treatment of adult patients with acute bacterial and skin structure infections (ABSSSI) caused by Gram-positive *Staphylococcus aureus* (specifically methicillin-resistant [MRSA] isolates) as an alternative oxazolidinione antibacterial. Treatment should only be initiated on advice from local microbiologists or specialists in infectious diseases.

Tedizolid phosphate (Sivextro®▼) is not recommended for use within NHS Wales outside of this subpopulation/circumstance.

The Chairman announced that confirmation of AWMSG's recommendations would be forwarded to applicant companies within five working days. He informed company delegates that they had up to ten working days to accept the recommendation or lodge a request for an independent review. It was noted that failure to respond within the deadline would not delay the process.

11. Appraisal 4 – Limited Submission

Raltegravir (Isentress®) in combination with other anti-retroviral medicinal products for the treatment of human immunodeficiency virus (HIV-1) infection in adults, adolescents, children, toddlers and infants from the age of 4 weeks

The Chairman welcomed representation from Merck Sharp & Dohme Ltd.

The Chairman reminded members to declare any interests in either the applicant company or the medicine if they had not already done so. No interests were declared.

The Chairman referred to his previous statement that AWMSG advice has no impact on the licensed status of the technology and the inherent implications associated with this. A negative recommendation would not impact on the clinical freedom of the prescriber. It was noted that a positive recommendation by AWMSG, subsequently endorsed by Welsh Government, places an obligation on Health Boards to fund accordingly. AWMSG advice is interim to final NICE guidance should this be subsequently published.

The Chairman confirmed that the application had been considered eligible for a limited submission and, in line with this process, evidence of budgetary impact against the existing comparator product should be demonstrated. The Chairman confirmed that if AWMSG makes a positive recommendation following appraisal of a limited submission, and it is subsequently ratified by Welsh Government, then monitoring budget impact would be essential. It was noted that AWMSG reserves the right to request a full submission if the budget impact exceeded that estimated in a limited submission.

The Chairman outlined the sequence of events and Mr Tony Williams, AWTTC Appraisal Lead, provided an overview of the submission as summarised in the ASAR and confirmed that the submission was eligible for a limited submission as it was considered a minor licence extension and likely to have a minimal budgetary impact within NHS Wales. Mr Williams informed members that the applicant company had suggested that any recommendation should be restricted to similar advice issued for other raltegravir indications. This would be for use in patients who are resistant or intolerant to non-nucleoside reverse transcriptase inhibitors or protease inhibitors, or for whom these options are compromised due to drug-drug interactions.

Mr Williams highlighted that there is currently a positive recommendation for the use of raltegravir for the tablet and chewable tablet formulations in children over two years of age and the focus of this submission is for the under two years age group.

Dr Al-Ismail confirmed that NMG had supported the use of raltegravir (Isentress®) 100 mg granules for oral suspension, in combination with other anti-retroviral medicinal products for the treatment of human immunodeficiency virus (HIV-1) infection in adults, adolescents, children, toddlers and infants from the age of four weeks as an option for restricted use within NHS Wales. Member were informed that NMG considered that raltegravir (Isentress®) 100 mg granules for oral suspension should be restricted for use in patients who are resistant or intolerant to non-nucleoside reverse transcriptase inhibitors (NNRTIs) or protease inhibitors (PIs), or for whom these options are compromised due to drug–drug interactions. NMG recommended that prescribers should consider switching from granules for oral suspension to chewable tablets when patient weight is ≥ 11 kg and should refer to the SPC for further information on the dosing of raltegravir (Isentress®).

The Chairman opened discussion. There were no issues in relation to clinical effectiveness. The Chairman referred to the budget impact. Some uncertainties in the assumptions were noted – members were reassured that due to the very low numbers of children with HIV in the Welsh population, it would be unlikely that this would have a significant impact on the budget impact estimations. It was noted that the medicine is available in Scotland and recommended in national guidelines. Mr Williams relayed the view of clinical experts that having access to a variety of medicines is important as it enables the clinician to construct treatment regimens that are suitable for the vast majority of patients. Mr Palmer highlighted the salient issues in the patient organisation submission received from the Terrence Higgins Trust. It was noted that the Terrence Higgins Trust supports the continued use of raltegravir as a treatment option for those starting treatment, with the caution that a thorough assessment of adherence is essential to ensure twice daily dosing is achievable.

The Chairman referred to the applicant company's response and offered further opportunity for the company delegate to comment prior to concluding the appraisal. The delegate had no further comment. Having received confirmation that the appraisal process had been fair and transparent and that all relevant issues had been discussed, the Chairman closed the appraisal.

Appraisal decision subsequently announced in public:
The Chairman confirmed that having read the evidence and considered the various issues that arose during the discussion, the following recommendation would be forwarded to Welsh Government:

Raltegravir (Isentress®) 100 mg granules for oral suspension, in combination with other anti-retroviral medicinal products for the treatment of human immunodeficiency virus (HIV-1) infection in adults, adolescents, children, toddlers and infants from the age of four weeks are recommended as an option for restricted use within NHS Wales.

Raltegravir (Isentress®) 100 mg granules for oral suspension should be restricted for use in patients who are resistant or intolerant to non-nucleoside reverse transcriptase inhibitors (NNRTIs) or protease inhibitors (PIs), or for whom these options are compromised due to drug–drug interactions.

The Chairman announced that confirmation of AWMSG's recommendations would be forwarded to applicant companies within five working days. He informed company delegates that they had up to ten working days to accept the recommendation or lodge a request for an independent review. It was noted that failure to respond within the deadline would not delay the process

12. Appraisal 5 – Limited Submission

Adalimumab (Humira®) for the treatment of severe chronic plaque psoriasis in children and adolescents from 4 years of age who have an inadequate response to or are inappropriate candidates for topical therapy and phototherapies

The Chairman welcomed delegates from Abbvie Ltd.
The Chairman reminded members to declare any interests in either the applicant company or the medicine if they had not already done so. No interests were declared.

The Chairman referred to his previous statement that AWMSG advice has no impact on the licensed status of the technology and the inherent implications associated with this. A negative recommendation would not impact on the clinical freedom of the prescriber. It was noted that a positive recommendation by AWMSG, subsequently endorsed by Welsh Government, places an obligation on Health Boards to fund accordingly. AWMSG advice is interim to final NICE guidance should this be subsequently published.

The Chairman confirmed that the application had been considered eligible for a limited submission and, in line with this process, evidence of budgetary impact against the existing comparator product should be demonstrated. The Chairman confirmed that if AWMSG makes a positive recommendation following appraisal of a limited submission, and it is subsequently ratified by Welsh Government, then monitoring budget impact would be essential. It was noted that AWMSG reserves the right to request a full submission if the budget impact exceeded that estimated in a limited submission.

The Chairman outlined the sequence of events and Mrs Sue Cervetto, AWTTC Appraisal Lead, provided an overview of the submission as detailed in the ASAR. Mrs Cervetto confirmed that the application had been considered eligible for a limited submission as it was a minor licence extension with anticipated minimal budgetary impact within NHS Wales. It was noted that no comparators were included in the company submission as there are no other biologic treatments currently recommended in Wales for use in the treatment of paediatric psoriasis. Dr Saad Al-Ismail confirmed that NMG had undertaken the preliminary appraisal in October and had recommended that adalimumab be made available as an option for use within NHS Wales for the indication being considered. He relayed the view of NMG that use should be in accordance with the National Institute for Health and Care Excellence (NICE) guidance for adults.

The Chairman opened discussion and clarification was sought in relation to wastage and vial sharing. Members explored the availability of quality of life and safety data. The company delegates confirmed some quality of life data was available from the paediatric study and no further safety signals to that already associated with other biologic therapies had been identified in the study population. Members recognised the distress of this condition on patients and their families. Mrs Cervetto relayed the views of clinicians as outlined in the clinical expert summary. A lack of provision of inpatient and day treatment was highlighted. It was noted that the only other licensed biologic intervention for children is etanercept and this medicine is currently not endorsed for use within NHS Wales as the marketing authorisation holder had not submitted an application for appraisal by AWMSG. Mr Palmer confirmed that two patient organisation questionnaires had been received, one from Psoriasis and Psoriatic Arthritis Alliance and one from Psoriasis Association. The Chairman confirmed that all members had received and read the patient organisation submissions and, in the interests of transparency, invited Mr Palmer to relay their views. Mr Palmer shared the experiences and highlighted the advantages to patients such as acceptable safety profile, convenient to use, good efficacy, less frequent dose regime and less intrusion on daily life. The psychological impact and physical symptoms of the condition were considered. There was discussion in relation to the inclusion of patients into a registry, and the company delegates confirmed they would be supportive of this.

The Chairman referred to the applicant company's response and offered further opportunity for the company delegate to comment prior to concluding the appraisal. The delegates had no further comment. Having received confirmation that the appraisal process had been fair and transparent and that all relevant issues had been discussed, the Chairman closed the appraisal.

Appraisal decision subsequently announced in public:
The Chairman confirmed that having read the evidence and considered the various issues that arose during the discussion, the following recommendation would be forwarded to Welsh Government:

Adalimumab (Humira®) is recommended as an option for restricted use within NHS Wales for the treatment of severe chronic plaque psoriasis in children and adolescents from 4 years of age who have had an inadequate response to, or are inappropriate candidates for, topical therapy and phototherapies. Prescribing should be restricted to clinical situations as specified within the National Institute for Health and Care Excellence (NICE) guidance for adults.

The Chairman announced that confirmation of AWMSG's recommendations would be forwarded to applicant companies within five working days. He informed company delegates that they had up to ten working days to accept the recommendation or lodge a request for an independent review. It was noted that failure to respond within the deadline would not delay the process

The meeting closed for a lunch break. Dr Emma Mason, Mr Scott Peglar and Dr Geoffrey Carroll left the meeting.

13. Appraisal 6 – Limited Submission

Tinzaparin sodium (Innohep®) for the extended treatment of symptomatic venous thromboembolism and prevention of its recurrence in patients with solid tumours

The Chairman welcomed delegates from LEO Pharma.

The Chairman reminded members to declare any interests in either the applicant company or the medicine if they had not already done so. No interests were declared.

The Chairman announced that AWMSG advice has no impact on the licensed status of the technology and the inherent implications associated with this. A negative recommendation would not impact on the clinical freedom of the prescriber. It was noted that a positive recommendation by AWMSG, subsequently endorsed by Welsh Government, places an obligation on Health Boards to fund accordingly. It was confirmed that AWMSG advice is interim to final NICE guidance should this be subsequently published.

The Chairman confirmed that the application had been considered eligible for a limited submission and, in line with this process, evidence of budgetary impact against the existing comparator product should be demonstrated. The Chairman confirmed that if AWMSG makes a positive recommendation following appraisal of a limited submission, and it is subsequently ratified by Welsh Government, then monitoring budget impact would be essential. It was noted that AWMSG reserves the right to request a full submission if the budget impact exceeded that estimated in a limited submission.

The Chairman outlined the sequence of events and invited Mrs Gail Woodland, AWTTC Appraisal Lead, to set the context of the appraisal. Mrs Woodland presented an overview of the submission as detailed in the ASAR and confirmed that the application had been

considered eligible for a limited submission as the anticipated usage was considered to be of minimal budgetary impact and there is an estimated small difference in cost compared to other available treatments.

The Chairman opened discussion. There was discussion in relation to shared care and an acknowledgement that these arrangements differ across Wales. Members discussed the dose alteration required with dalteparin after one month of treatment. Mrs Woodland relayed the views of clinical experts and it was noted that no unmet need had been identified; however clinical experts indicated that they would replace or consider replacing their current choice of low molecular weight heparin with tinzaparin if it was cheaper. There were no issues relating to the budget impact and no wider societal issues of note. Mr Palmer confirmed that three patient organisations had been approached; however, no submissions had been received.

The Chairman referred to the applicant company's response and offered further opportunity for the company delegate to comment prior to concluding the appraisal. The delegates had no further comment. Having received confirmation that the appraisal process had been fair and transparent and that all relevant issues had been discussed, the Chairman closed the appraisal.

Appraisal decision subsequently announced in public:
The Chairman confirmed that having read the evidence and considered the various issues that arose during the discussion, the following recommendation would be forwarded to Welsh Government:

Tinzaparin sodium (innohep® Syringe) is recommended as an option for use within NHS Wales for the extended treatment of symptomatic venous thromboembolism and prevention of its recurrence in adult patients with solid tumours.

The Chairman announced that confirmation of AWMSG's recommendations would be forwarded to applicant companies within five working days. He informed company delegates that they had up to ten working days to accept the recommendation or lodge a request for an independent review. It was noted that failure to respond within the deadline would not delay the process

14. Feedback from AWPAG Meeting held 23rd September 2015

The draft minutes of the AWPAG Meeting held in September 2015 were provided for information.

15. All Wales Policy for Medicines Administration, Recording, Review, Storage and Disposal

Mrs Louise Williams presented Enc **11/**AWMSG/1115, an All Wales Policy for Medicines Administration, Recording, Review, Storage and Disposal (MARRS). It was noted this project is pertinent to the following recommendations of the AWMSG Five-year Strategy 2013–2018:

Recommendation 2: Improving health – Prescribing guidance
AWMSG will work with health boards and other stakeholders to promote the safe, effective and cost-effective use of medicines in Wales.

Recommendation 4: Fully integrated network of care
AWMSG will work with stakeholders so that care can be delivered in the most appropriate setting.

Mrs Williams informed members that the All Wales Policy for Medicines Administration, Recording, Review, Storage and Disposal (MARRS) had been developed via a joint working group in response to medicines practice issues identified as part of the Trusted to Care report published in 2014. It provides a standards framework for health boards and trusts in Wales.

Mrs Williams clarified the purpose of the policy is to set out the minimum standards of practice that must be adopted by all healthcare employees involved in the administration, recording, review , storage and disposal of medicines in Welsh hospitals. The implementation of these standards will ensure that medicine administration and practices are of a consistently high standard and patients, staff and visitors to Welsh hospitals are protected from the harmful effects of medicines through robust medicines storage practices.

The Chairman invited comment. There was a suggestion that the same standards should be applied within nursing homes. Mrs Williams confirmed the terms of reference of this project applied to the managed sector. Members welcomed the policy and were encouraged that mandatory training, education and output in relation to medicines administration would be consistent across NHS Wales. The Chairman confirmed AWMSG's endorsement.

16. All Wales Guidance for Health Boards/Trusts in Respect of Medicines and Health Care Support Workers

Mrs Williams presented Enc **12**/AWMSG/1115 All Wales Guidance for Health Boards/Trusts in Respect of Medicines and Health Care Support Workers. Mrs Williams highlighted the purpose of the guidance is to set out a framework to standardise the involvement of the health care support worker (HCSW) in processes involved in medicines management and to ensure that only appropriately trained HCSWs, with the right knowledge and skills, provide support with medication and its related tasks. The practice undertaken must be in accordance with locally agreed written protocols and procedures for designated settings where health boards/trusts have a responsibility for providing care. The aim of the guidance is to ensure practice is robust, safe and of equitable standard throughout the principality. The guidance was developed via a joint working group with representation from the Chief Nursing Officer, Nurse Directors Wales, Chief Pharmaceutical Officer, All Wales Chief Pharmacist Group and Medical Directors. It is intended that the guidance would be implemented within four months following formal consultation and endorsement. The guidance is intended to inform health boards/trusts on the level of support provided by HCSWs within medicines administration, permitted medicines, educational and training requirements, and appropriate governance arrangements. The document is aligned to the NHS Wales Careers and Skills Framework for HCSWs.

The Chairman invited comment. Members welcomed the guidance and supported its development.

The meeting was closed to members of the public because of the confidential patient access scheme associated with the denosumab (Xgeva®) submission.

17. Appraisal 7 – Limited Submission (PAS)

Denosumab (Xgeva®) for the treatment of adults and skeletally mature adolescents with giant cell tumour of bone that is unresectable or where surgical resection is likely to result in severe morbidity

The Chairman welcomed delegates from Amgen Limited.

The Chairman reminded members to declare any interests in either the applicant company or the medicine if they had not already done so. No interests were declared.

The Chairman announced that AWMSG advice has no impact on the licensed status of the technology and the inherent implications associated with this. A negative recommendation would not impact on the clinical freedom of the prescriber. It was noted that a positive recommendation by AWMSG, subsequently endorsed by Welsh Government, places an obligation on Health Boards to fund accordingly. It was confirmed that AWMSG advice is interim to final NICE guidance should this be subsequently published.

The Chairman confirmed that the application had been considered eligible for a limited submission and, in line with this process, evidence of budgetary impact against the existing comparator product should be demonstrated. The Chairman confirmed that if AWMSG makes a positive recommendation following appraisal of a limited submission, and it is subsequently ratified by Welsh Government, then monitoring budget impact would be essential. It was noted that AWMSG reserves the right to request a full submission if the budget impact exceeded that estimated in a limited submission.

The Chairman outlined the sequence of events and Mrs Helen Adams, AWTTC Appraisal Lead, presented an overview of the submission as detailed in the ASAR. Mrs Adams confirmed that the limited criteria were met as the anticipated usage of denosumab in NHS Wales was considered to be of minimal budgetary impact. Dr Al-Ismail confirmed that NMG had appraised this medicine in October and supported its use within NHS Wales. No patient organisation submission had been received. Clinical experts highlighted that medical management of locally advanced, destructive giant cell tumours is currently unsatisfactory. They considered denosumab to be a significant improvement over current therapy. The Chairman opened discussion. Clarification was sought in relation to the treatment course and the criteria for discontinuing treatment. There were no budget impact issues of note. The Chairman expressed disappointment that five patient organisations had been approached but no questionnaires had been received.

The Chairman referred to the applicant company's response and offered further opportunity for the company delegate to comment prior to concluding the appraisal. The delegates had no further comment. Having received confirmation that the appraisal process had been fair and transparent and that all relevant issues had been discussed, the Chairman closed the appraisal.

Appraisal decision subsequently announced in public:
The Chairman confirmed that having read the evidence and considered the various issues that arose during the discussion, the following recommendation would be forwarded to Welsh Government:

Denosumab (Xgeva®) is recommended for use within NHS Wales for the treatment of adults and skeletally mature adolescents with giant cell tumour of bone that is unresectable or where surgical resection is likely to result in severe morbidity. This recommendation applies only in circumstances where the approved Patient Access Scheme is utilised.

The Chairman announced that confirmation of AWMSG's recommendations would be forwarded to applicant companies within five working days. He informed company delegates that they had up to ten working days to accept the recommendation or lodge a request for an independent review. It was noted that failure to respond within the deadline would not delay the process.

The Chairman confirmed the date of the next meeting on **Wednesday, 9th December 2015 in Abergavenny** and closed proceedings.